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LOEFFLER'S SYNDROME ASSOCIATED WITH ASCARIS LUMBRICOIDES

Case Report No. 84

Dr. Hugh Clark

J. J. 43-166

J. J., a four year old colored male, was admitted to the hospital on September 22, 1946 with a history of convulsions.

On the day of admission the boy had had a tonic seizure involving the upper extremities. There was no associated loss of consciousness during the attack. The temperature prior to the onset of the convulsions had been normal. Three months prior to entry patient had had a similar seizure lasting about two hours, was hospitalized for five days, and was treated for whipworms and pharyngitis.

Past history revealed measles in April, 1946 with an uneventful recovery. There had been no other significant illnesses. The birth and developmental history were normal and as far as known, there was no allergic diathesis.

The family history was negative for tuberculosis, malignancy, syphilis, diabetes and convulsions.

Physical examination revealed a well developed, well nourished, four year old colored male, who was cooperative and well oriented. The sensorium at this time was clear. The physical findings including the neurological examination, were not remarkable. Repeated hemograms following admission showed a moderate anemia, leucocyte count ranged between 5,900 and 11,300, eosinophil counts ranged between 4 and 21% with an average of 12%. Urinalyses were negative. The blood sugar on the day following admission was 80 mgm.%. No sickling of the red blood cells was noted. The blood serology was negative. Eight stool examinations for ova and parasites were performed and of these, six were negative, one was positive for *Ascaris lumbricoides*, and one showed the ova of *Trichuris trichiura*. The sedimentation rate was within normal limits and heterophile agglutination was negative in all dilutions. A tuberculin test (P.P.D. #2) was minimally positive. Examination of three concentrated specimens of gastric contents was negative for tubercle bacilli. A nasal smear did not show an excessive number of eosinophils. Similarly, several sputum examinations were negative for eosinophils and *Ascaris* larvae. Negative skin tests were reported for the common inhalant allergens but the *Ascaris* skin test was positive.

X-rays of the chest were taken on seven different occasions. The first film taken two days after admission to the hospital showed an infiltration in the second, third, and fourth interspaces anterior in the right

and left lung with increased hilar markings. Five days later there was a hazy infiltration through the lower two thirds of the left lung field. Subsequent films showed a transient migratory character to the infiltration which resolved on October 18th. The roentgenogram taken on that day

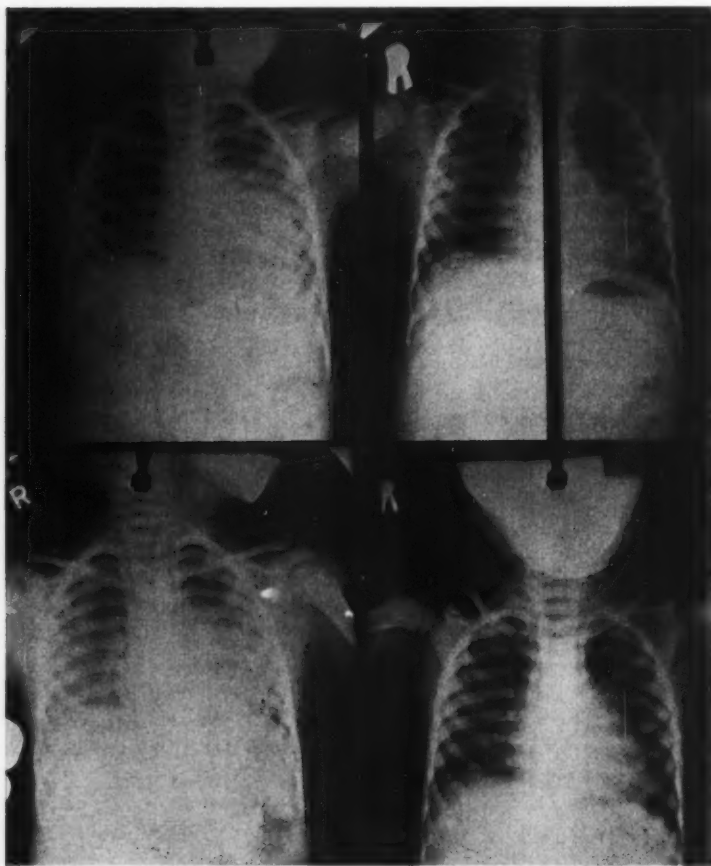


FIG. 1. Note shifting areas of infiltration with eventual resolution after one month.

revealed a rather dense shadow in the right hilar region which was interpreted as representing an enlarged gland associated with an increase in peribronchial markings indicative of a bronchitic condition; the previously described infiltration had undergone resolution.

The course of this patient was entirely uneventful. He was never really

ill. There was never any striking pulmonary physical signs. His temperature ranged between normal and 100°F. His treatment consisted of a course of anthelmintic and supportive therapy. He was discharged on October 21 as improved and he is to be followed up in the out-patient department.

DISCUSSION

Bernard Rosenberg: This case, with its transient pulmonary infiltrations, eosinophilia, mild clinical course, and variable x-ray findings, fleeting and migratory, out of proportion to the mild signs and symptoms, is characteristic of Loeffler's syndrome.

In 1932 and again in 1936, Loeffler reported a syndrome characterized by transitory pulmonary infiltrations, blood eosinophilia varying from less than 10% to more than 60%, a mild clinical course which was in striking contrast to the extensive pulmonary lesions, transient and migratory, as seen in the x-rays, and spontaneous healing usually within a period of two to three weeks.

The etiology of Loeffler's syndrome is obscure. There is increasingly convincing evidence, however, that this disease is really an allergic sensitization in which the interstitial tissue of the lung is the shock organ.

Loeffler originally considered that the condition might be a benign atypical form of pulmonary tuberculosis. Maier reviewed a hundred cases at Loeffler's clinic in Zurich and found only two patients with active tuberculosis at the time of the illness. He later considered the role played by parasites causing the condition and thought that the eosinophilia was an expression of an anaphylactic process.

The first important contribution to the etiology of the syndrome is probably that of Engel, who had observed seasonal occurrences of cough in Shanghai which coincided with the flowering of the privet plant in May and June. Most of the cases of Loeffler's syndrome occurred in July and August. Soon the list of diversified causes came to be known and the true nature of the syndrome to be recognized. The factors tending to favor an allergic hypothesis are the following: transient nature of the pulmonary lesions, minimal disturbance of health in the presence of extensive pulmonary lesions, peripheral and sputal eosinophilia, absence of infection (usually normal leucocyte count, sedimentation rate, temperature, absence of systemic manifestations), normal vital capacity, short mild clinical course, family history of allergy, associated allergic phenomena—in 52 out of 100 cases—such as eczema, hay fever, migraine, vasomotor rhinitis, urticaria, asthma, either before or at the time of the illness, and a diversified list of etiologic factors.

Swiss observers have emphasized the rather frequent association of the syndrome with *Ascaris* infestation. Zweifel found sensitivity to *Ascaris*

extract in 70% of the cases with Loeffler's syndrome, whereas normal persons, persons with ascariasis and allergic persons reacted to it in only 40%. Zweifel concluded that, while *Ascaris* appears to be the most frequent cause of these pulmonary infiltrations, it is not the exclusive allergen.

Cases have been reported in which Loeffler's syndrome has apparently been due to the following:

1. Worm infestations
 - a. *Ascaris lumbricoides*
 - b. *Strongyloides stercoralis*
 - c. *Trichinella spiralis*
 - d. *Ancylostome braziliense*
 - e. *Necator americanus*
 - f. Liver fluke
2. Asthma
3. Brucellosis
4. *Entameba histolytica*
5. Pollinosis
6. Sulfonamides
7. Gold Salts

The syndrome appears to represent a genuine allergic phenomenon, the pulmonary tissues constituting the shock organ. Gravesen stresses that it is the interstitial tissue of the lung that is hypersensitive rather than the bronchi, as is the case in asthma.

The cases in which ascariasis appears to be the cause raise the question whether the pulmonary infiltrations represent a purely allergic inflammatory reaction in response to the *Ascaris* toxin or whether the pulmonary infiltrations are the response of invasion of the lungs by the larvae of the helminth. Most observers, including Maier and Weber, failed to find the larvae of the ascarids in the sputum. The only support for the thesis of this being *Ascaris* larva pneumonia is the experiment of Koino, in which this investigator swallowed 2,000 larval eggs of ascarids with resultant migrating pneumonic consolidation and sputum containing larvae. This experiment of course, is not necessarily comparable to the natural evolution of the disease.

In summing up the conclusions in the more recent literature, one is led to the conclusion that Loeffler's syndrome is an allergic reaction that can be produced by a variety of allergens.

This case is probably on the basis of allergy to *Ascaris lumbricoides*.

PATHOLOGY

Since the clinical course in Loeffler's disease is mild and since spontaneous healing takes place, autopsy material is rarely available. According to Loeffler's early reports, the pathogenesis is similar to erythema nodosum,

the lung reacting with an inflammatory exudate to a toxin. Engel believes that a localizing allergic edema of the lungs is responsible for the entire picture.

Pathologic observations on this condition are limited to post-mortem studies by Von Meyenburg on four accidental deaths. He found that the infiltrations were of pneumonic type with exudation into the alveoli and the interstitial tissue. There was also an inflammatory involvement of the pleura and the interlobar fissures. Von Meyenburg failed to demonstrate tubercle bacilli or *Ascaris* larvae in the pulmonary tissue.

Bayley and his associates recently reported the results of the post-mortem examination of a woman aged fifty-nine who died with Loeffler's syndrome. The bronchial lesions were similar to those observed in bronchial asthma. They found some infiltrates in advanced organization and concluded that the pulmonary lesions are not "transitory" in all cases. The most striking vascular change was that of necrotizing arteritis and arteriolitis, quite similar to the change observed in periarteritis nodosa.

CLINICAL MANIFESTATION

There may be no symptoms. Often the syndrome is discovered in the course of a routine examination. There may be mild cough, occasionally some expectoration or scanty sputum, mild chest or pleural pain, and some fatigue. Not uncommonly asthmatic breathing is noted. Some authors report a metallic taste to the sputum as a fairly frequent occurrence. At times, there are acute severe symptoms almost like those of a septic process.

In this case a mild cough of one day's duration was noted as a secondary complaint. There was nothing to point to the respiratory system as a site of marked pathological changes. This patient was not ill. The two convulsions probably have no relation to the pulmonary infiltrations. Their cause is uncertain, but may be due to the presence of intestinal parasites in an unusually susceptible individual or perhaps to an idiopathic epilepsy.

The physical signs are usually a few in number, as is the case with other interstitial diseases. Decreased breath sounds and moist or sibilant rales over the areas of infiltration are the commonest auscultatory evidence and these are only occasionally present. Generally speaking, there is a paucity of physical signs when compared with the extensiveness of the infiltration as shown by x-ray. The temperature may be normal or moderately elevated. A low-grade fever is just as often absent as it is present. This patient had no physical signs in the chest. He did, on occasion, have a low-grade fever.

The outstanding laboratory finding is the blood eosinophilia which ranges from 6% to over 60%. One case has been reported with an eosino-

philia of 85%. However, the average is 10-30%. There appears to be no strict relationship between the extent of the pulmonary infiltrations and the grade of eosinophilia. Usually, the eosinophilia is maximal when the pulmonary lesions are maximal and thus cannot be regarded as a post-infectious phenomenon, but in some instances the eosinophilia reaches a peak when the pulmonary infiltrations have almost completely disappeared. The eosinophilia may persist for variable periods, as long as nine months in several instances. Jones and Souders do not consider the eosinophilia as essential for making the diagnosis, since it may be absent or be depressed by associated infection. Some authors have reported finding eosinophils in the sputum. The leucocyte count may be normal or may show a mild leucocytosis. The sedimentation rate is usually increased. All tests for tuberculosis are negative. This case showed an eosinophilia ranging between 4% to 21%, averaging 12%. No eosinophils were found in the sputa examined. The white blood cell count and sedimentation rate were within normal limits. The tuberculin tests and gastric washings were negative.

ROENTGEN FEATURES

The essential and distinguishing feature of the syndrome as emphasized by Loeffler is the fleeting, migratory character of the pulmonary infiltrations. The main characteristics of the infiltrates are the sudden appearance, with complete disappearance within 3-8 days. They are of variable size, density, and distribution. There is no distinctive pattern. The infiltrations may be extensive and irregular in shape or they may be small and round, resembling the shadows of primary tuberculous infiltration; they may be fleecy or dense, unilateral or bilateral; they may involve the entire lung or be limited to one lobe. Loeffler stressed as the characteristic x-ray picture consolidations which appear suddenly in various parts of the lung and disappear rapidly while others appear in another portion of the lung. Spector believes that the shadows are more frequently found in the lower lung fields near the diaphragm. Hennell and Sussman state that there is no predilection for upper or lower lobes, but a fair degree of symmetry on the two sides is the rule. The infiltrates rarely persist in any one place for more than eight days. Complete resolution usually takes place, but a few linear or fine fibrous star-shaped strands may remain. Breton points out that in some cases the x-ray shadows tend to recur. In a small number of cases Loeffler observed involvement of the pleura with occasional small circumscribed pleuritic effusion.

This patient first showed infiltrations in the upper lung fields of both sides, then in the lower left field, then hilar involvement, next lower left and lower right lung fields, next retrocardiac, and finally hilar involvement. All these changes occurred in the space of one month.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of Loeffler's syndrome can only be made, first by the blood eosinophilia; second, by the transient x-ray shadows; and third, by the clinical course. An allergic history prior to onset of symptoms is an aid in diagnosis. Positive stool findings, whether amebae or other parasites, calls for blood studies and chest x-rays. Frequently a definite diagnosis can only be made through the medium of serial x-ray films of the lungs and after the condition has subsided.

In the differential diagnosis the following conditions must be considered: pulmonary tuberculosis, pulmonary embolism with infarction, pulmonary neoplasm, pneumonia, bronchiectasis, bronchial asthma with partial atelectasis, erythema nodosum, Hodgkin's disease, sarcoidosis, atypical virus pneumonitis, eosinophilic leukemia, and tropical eosinophilia. In this case the diagnostic requirements were adequately fulfilled. Tuberculosis was ruled out and the differential diagnosis was fairly simple. As a rule, there are no sequelae, as was the case in this patient. Occasional complications are right ventricular strain, pleural effusion, and asthma.

COURSE AND PROGNOSIS

There is usually spontaneous disappearance of physical signs, x-ray shadows and blood eosinophilia in a period of one to three weeks. A few cases have been reported where the condition lasted for a longer period with delayed recovery. Lohr and Kindberg have reported a type in which the acute symptoms are severe and the process is extremely protracted and persists for months. Kartagener described a case which he regards as representative of a third type of eosinophilic infiltration, characterized by chronicity and mildness of symptoms. In some of these protracted cases, the pulmonary infiltrations remain demonstrable roentgenologically for many weeks or months. The prognosis is excellent. No fatalities have been reported.

TREATMENT

There is no specific therapy for Loeffler's syndrome. In treating this condition successfully a search should be made for any specific allergen (whether it be an intestinal parasite or pollen as a direct or indirect cause of the condition) and the offending allergen should be removed. Bed rest and symptomatic treatment will aid in recovery of all other types of transient pulmonary infiltrations with eosinophilia. Weingarten in India recently reported that arsenicals are specific for tropical eosinophilia, which appears to be closely related to Loeffler's syndrome.

It can not be definitely stated that specific treatment for ascariasis

exerted a beneficial effect in this case, since the course ordinarily is so brief even without treatment.

CONCLUSIONS

A review of the literature leads to the conclusion that Loeffler's syndrome is an allergic phenomenon, usually in individuals with an allergic tendency, as the result of various allergens. Intestinal parasites are frequently found associated with Loeffler's syndrome; it is believed that this case is on the basis of *Ascaris lumbricoides*.

More recent investigations indicate that pathologically the condition represents an eosinophilic pneumonitis in which the interstitial tissue of the lung is the shock organ.

The outstanding findings in Loeffler's syndrome are the blood and sputal eosinophilia, the transient fleeting and migratory pulmonary infiltrations, the mild course, and the spontaneous healing without complications.

No specific treatment is known for the condition other than to remove the offending allergen.

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LEUKEMIA WITH AN ASSOCIATED SEPTICEMIA

Case Report No. 85

Ralph Stiller, M.D.

F. MacW. 46-9293

A three and one half year old white male was admitted to Children's Hospital on October 13, 1946 with the chief complaint of repeated nose bleeds and increasing pallor of 8 days duration.

The child had never been sick prior to this year. He was born after normal gestation, weighing $8\frac{1}{2}$ pounds with the delivery being entirely normal. He was well neonatally and was breast fed for seven months. At no time did he receive any cod liver oil or its dietary equivalent; orange juice intake was adequate. His developmental history was entirely normal.

His first illness occurred six months before his present admission when in April of this year he had chickenpox and during the ensuing months, he had in rapid succession influenza, measles and pertussis. In mid-August at about the time corresponding with his convalescence from pertussis, he developed an infection of his right heel which drained purulent material for about two weeks and was followed by gradual healing. By early September (6 weeks before admission) he was well, gaining weight, and normally active. Eight days before admission he developed a head cold associated with coughing, sneezing and moderately severe epistaxis. There were three recurrent episodes of epistaxis during the following week. The coughing and sneezing continued and in the last few days before hospitalization an increasing pallor was noted. He became progressively weaker, refused to eat, and for twenty-four hours before admission complained of pains in his legs. At no time was there any complaint of headache, tinnitus, or vertigo, or urinary symptoms.

Physical examination on admission revealed an acutely ill white male of three and a half years, looking extremely pale with a moderate degree of cyanosis visible on the lips and nail beds. The temperature was 104° . Positive physical findings included dry, swollen and spongy gums with no apparent bleeding points. The tongue was dry and coated, the tonsils small, ragged, congested. The teeth were carious. The thorax was symmetrical and respirations were easy. A few fine scattered rales were heard over both lung fields and there were superimposed coarse rhonchi. The heart was normal except for a soft systolic blow heard at the base which was thought to be functional. The blood pressure was 106/86. Abdominal examination revealed some diffuse mild tenderness with no localization. The liver was palpable 6 cm. below the costal margin, the splenic tip was felt 2 cm. below the costal margin. His skin was extremely pale, hot and dry. All nodes were mildly enlarged and discrete.

There was a non-pitting swelling of the legs from the lower third of the tibia to the toes.

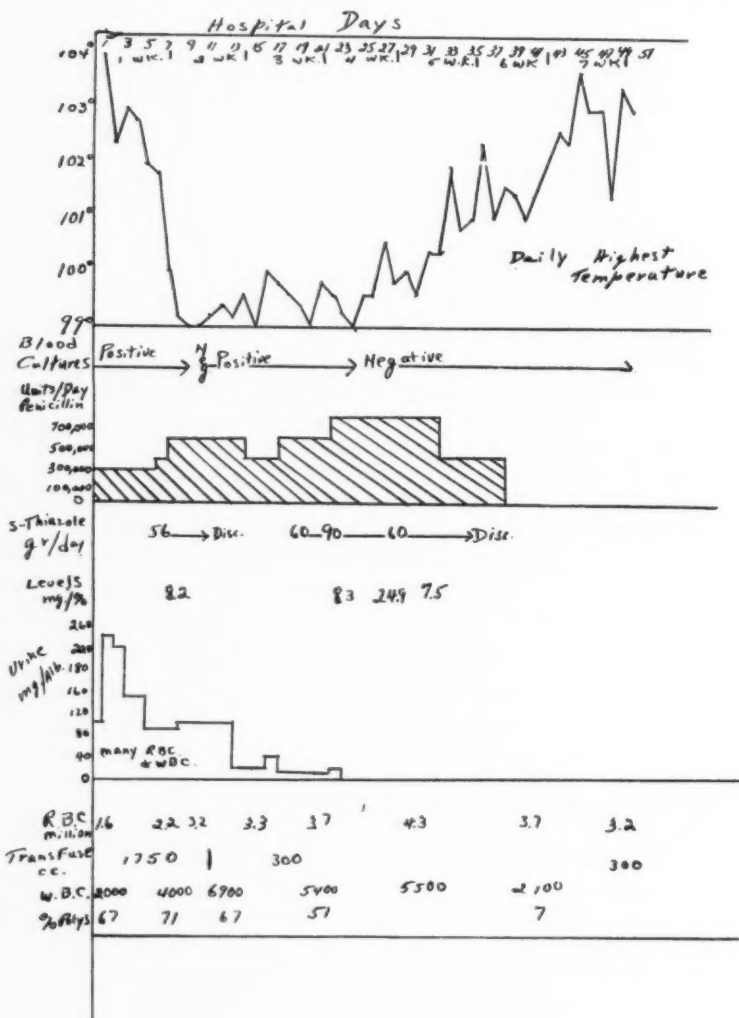


FIG. 1

Admission laboratory work revealed a hemogram of 1.6 million with a hemoglobin of 5 gms.; the white cell count was 2,000 with 67% neutro-

phils of which 55% were segmented forms and 33% lymphocytes. The thrombocyte count was 40,000.

Urinalysis was cloudy with a specific gravity of 1.016. Sugar and acetone were negative. There was 100 mgm.% of albumin. Microscopic examination revealed numerous erythrocytes and a moderate number of white blood cells.

For the first six hospital days the course of this child's illness was characterized by a temperature that irregularly spiked up to 103° daily and was associated with a constantly changing clinical picture. The pulmonary findings became more prominent with an increase in the number and loudness of the rales heard bilaterally. Repeated laboratory examinations confirmed the urinary and blood findings. A bleeding and coagulation time was reported as normal. The abdomen became distended and the liver and spleen became progressively larger until by the fourth hospital day, the former was palpable below the level of the umbilicus and the latter 6 cm. below the costal margin. On the third hospital day several purpuric areas appeared on the back and in the loins. It was noted that there was dried blood on the child's lips although the previously mentioned spongy gums showed no signs of bleeding. A Rumpel-Leede capillary fragility test was done and showed increased capillary fragility. Radiographic examination of the lungs and heart the day after admission revealed the heart to be at the upper limits of normal in size. There was a considerable increase in the bronchovascular markings throughout the parenchyma particularly in the right base which was interpreted as being consistent with the diagnosis of a low-grade bronchopneumonia.

Several diagnoses were considered at this stage in the development of the disease and so for empirical reasons the patient was given 40,000 units of penicillin every 3 hours, frequent transfusions and oxygen when necessary. Pneumonia, glomerulonephritis with concomitant heart failure, leukemia, aplastic anemia (either primary or secondary to an acute infection) and septicemia were all considered. A venous pressure was done on the third hospital day and was reported as 40-60 mm. water with no increase on compression of the enlarged liver. As this is a normal reading, it was felt that the possibility of heart failure was less likely. Several blood cultures were taken and a sternal marrow biopsy was done. On the fourth hospital day the blood culture taken earlier was reported as positive with 450 colonies per cc. of hemolytic *Staphylococcus aureus*. A penicillin sensitivity on these organisms was reported as 14% with 100% being maximum sensitivity. At the same time the marrow biopsy was interpreted as compatible with a toxic suppression of all the blood elements.

With *Staphylococcus septicemia* as a working diagnosis and with indications of a relatively penicillin fast organism, the dose of penicillin was raised to 75,000 units every 3 hours and sulfathiazole was given in a dosage

level of 2 grains per pound of body weight. Improvement up to a point was encouraging. The temperature came down by lysis and was completely normal throughout the second hospital week. The liver and spleen both receded until the former was but 1 finger below the costal margin and the latter could not be palpated. The chest signs completely cleared up and the child appeared less toxic. Urinary findings became negative, except for some sulfathiazole crystals, by the third hospital week and with frequent transfusions the hemogram became stabilized at an average figure of 3.5 million red cells with a hemoglobin of 10.5 grams and a white cell count of about 5,500 with a normal differential. Despite these findings the blood cultures remained consistently positive with 1 to 5 colonies of *Staphylococcus aureus hemolyticus* growing in each pour plate. Because of the excellent clinical picture and the normal delay in blood culture reports (this organism invariably did not grow out until the 5th to 7th day) the sulfathiazole was discontinued and the penicillin reduced to 50,000 units every 3 hours during the second hospital week. Following this, slight daily febrile rises to 100 and 100.5° occurred. By the beginning of the fourth week the penicillin dosage had been raised to a total of 800,000 units a day and sulfathiazole was resumed. For a few days during the fourth week the temperature was normal but soon, despite the intensive therapy and with all cultures reported as negative since November 6, fever recurred, first low grade then in the range of 100–102° and finally up to 103°. All medication was discontinued, the sulfathiazole on November 16, the penicillin on November 19. A blood count taken November 22 showed 50,000 thrombocytes, 3.7 million red blood cells, a hemoglobin of 12.5 grams and a white blood cell count of 2,100. The differential smear was rather bizarre with only 7% granulocytes, 63% lymphocytes, and 29% immature mononuclear cells. Clot retraction time the next day was reported as normal but a bone marrow biopsy on November 24 gave a picture definitely consistent with leukemia of an undetermined type. With the definite diagnosis of leukemia it was felt that nothing could be gained by keeping the child in the hospital any longer. He was given a 300 cc. transfusion the day before discharge and sent home to return for further transfusion therapy when needed.

We have learned indirectly that the child died at home a few days after discharge. The exact nature of the terminal event is not known.

DISCUSSION

This case presented some very interesting problems in differential diagnosis and as can be seen, the working diagnosis eventually agreed on was not the whole story. We dealt here not with a particularly rare disease but with a patient who showed a complex of symptoms and signs referable

to virtually every system. Combinations could be worked out to account for any one of the various diagnoses considered but an attempt to explain everything on one basis along the classical lines of thinking brought one up against very definite difficulties. The hepatic and splenic enlargement, the discretely enlarged nodes, the purpura and the general blood picture on admission are all explainable quite easily by one or the other or both of the two final diagnoses, (i.e. septicemia and leukemia). I feel in retrospect that the urinary findings were due primarily to the septicemia; a transitory focal nephritis of the type seen in subacute bacterial endocarditis could well explain the picture. It was suggested that the urinary findings could be explained by intratubular bleeding on a leukemic basis but in view of the subsidence of these symptoms despite the leukemic exacerbation toward the end of the hospital course, this seems unlikely. The other set of symptoms, those referable to the lungs, is a little more difficult to explain. The possibility of a concomitant heart failure has been ruled out and all we have left is the rather simple explanation that the child had a moderately severe bronchopneumonia complicating his primary illness. How long the leukemic state had been in existence is hard to state with accuracy but it seems highly likely that the many bouts of illness that the patient had starting a full six months before his admission to the hospital were incident to his weakened state. His leukemia may well have been present throughout this entire period.

From the standpoint of the *Staphylococcus septicemia* a word might be said concerning therapy. This phase of the child's care was eventually successful although it was not until a dosage of penicillin approaching 1,000,000 units a day together with a 2 grain per pound dose of sulfathiazole were instituted that sterile blood cultures were obtained. If this had failed, the only other alternative would have been to establish a continuous drip of penicillin over a prolonged period of time. It is well to note here that the laboratory report of a relatively penicillin fast organism did not discourage treatment with penicillin; it only prompted the raising of the dosage to higher levels. This might be a good plan to follow in other similar cases. It is debatable whether any foci of infection in the form of scattered abscesses were still present. Prior to the establishment of the final diagnosis it was felt that the febrile curve toward the end of hospitalization was explainable on this basis. However, leukemia per se could well cause this and the presence or absence of abscesses becomes of academic importance only.

FATALITY DUE TO ASCARIASIS

Case Report No. 86

Frances Ayres, M.D.

C. L. W. 46-7635

C. L. W., a 2 year old colored female, was admitted to Children's Hospital because of difficult breathing. The present illness began 3 days previously with the onset of a cold manifested chiefly by rhinorrhoea. The night before admission, the child began to cough and the mother noticed difficulty in breathing. No fever was noted during this time and there was no vomiting or diarrhea.

The past history was unrevealing. The delivery was normal after a one hour labor. The development was normal. She walked and talked at 12 months. She was receiving a general diet and breast milk, but had never had any supplementary vitamins. She had measles at 1 year and occasional colds, but no other illnesses. The child had received no immunizations. The family history was non-contributory.

At the time of admission, the patient was acutely ill, cyanotic and in marked respiratory distress. Her temperature was 103° and her respirations were 35. The physical findings were limited to the chest and abdomen. In both lung fields there were numerous fine moist rales. The abdomen was moderately distended and the liver was palpable 1.5 cm. below the right costal margin. A diagnosis of bronchopneumonia was made and treatment was initiated consisting of continuous oxygen and penicillin. Her respirations became more rapid and labored and she died four hours after admission.

The autopsy findings in this case were unusual. During the external examination, an ascarid was noted in the external nares. The mediastinal and bronchial lymph nodes were found to be enlarged and on sectioning, caseous material was expressed. The right lung showed areas of emphysema and consolidation. The left upper lobe was atelectatic and there were two subpleural tubercles at the base. Microscopic examination confirmed the gross diagnosis of atelectasis, emphysema, pneumonitis and tuberculosis. A rather marked eosinophilic infiltration of the lung was noted.

Examination of the abdominal contents revealed evidence of tuberculosis as well as massive infestation with *Ascaris lumbricoides*. The microscopic examination of the liver showed an extensive tuberculous process in that organ. The sections of spleen were also suggestive of early tuberculosis. The gastrointestinal tract appeared normal externally. However, when the upper end of the esophagus was severed at the level

of the larynx, several ascarids each approximately 4 inches long escaped from its lumen. There were a few parasites in the pyloric end of the stomach, and the intestinal lumen from the pyloric end of the stomach to

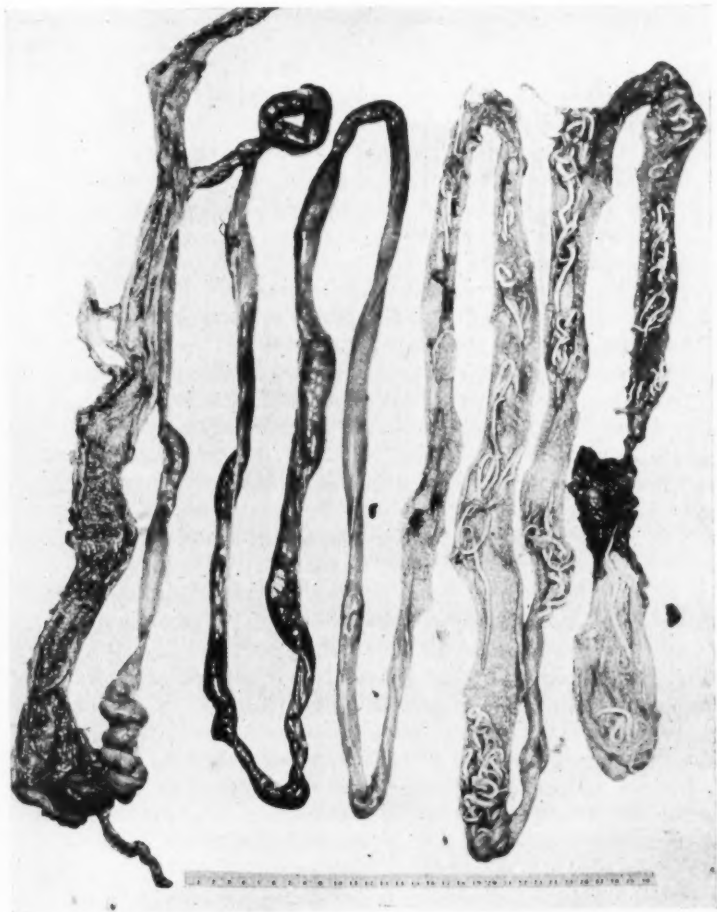


FIG. 1. Small bowel showing numerous adult worms

the ileo-cecal valve was filled with at least several hundred adult ascarids which were matted together. The infestation was most marked in the small bowel, there being only an occasional parasite in the colon. The

intestinal tract was patent throughout and there was no apparent damage to the mucosa.

DISCUSSION

The immediate cause of death in this child can not be stated with certainty. There was extensive involvement of the lungs by a pneumonic process, probably tuberculous, which could have been contributory. There was also evidence of disseminated tuberculosis so that an early military tuberculosis could have been the cause of her death. It is also possible that the heavy parasitic infestation was the responsible or at least an important factor. The finding of ascaris in the upper esophagus and in the external nares presents the rather remote possibility of asphyxiation. The amount of toxins liberated by the parasites might have made her more susceptible to the infection, reducing her resistance to the invader. Whatever the immediate cause of death might have been, certainly it is that the most striking and unusual aspect of this case is the heavy *Ascaris* infection, and it is that aspect of the case which will be discussed.

To better understand the clinical side, a brief review of the parasitology and pathogenicity of *Ascaris* will be presented. This parasite is a cylindrical worm varying in length from 15 to 40 cm, the males being smaller than the females. The organs in the coelomic cavity are bathed in a liquid which contains Ascaron, the *Ascaris* toxin. The usual habitat of this parasite is the small intestine of man. In the usual case of Ascariasis, there are 8 to 10 worms present, but occasionally, there may be well over a thousand. The life cycle of this parasite is as follows: eggs are passed in the human feces and the embryo develops outside the body and then is ingested by man. In the intestine the embryo becomes active, goes through the intestinal wall to the liver where it stays for three or four days. It then migrates to the lungs where it causes a pneumonitis, and then passes by way of the bronchi and trachea to the gastrointestinal tract where it matures. The pathogenicity of *Ascaris* infection in man is due to a variety of causes. The parasite may take blood or chyme from the host; its toxin may cause nervous or allergic reactions; it may traumatize the bowel wall; it may occlude ducts such as the biliary duct; also it may cause intestinal obstruction or go to the larynx and cause asphyxia.

Swartzwelder in an analysis of 202 patients with clinically evident Ascariasis listed the following as the most common symptoms of *Ascaris* infestation: abdominal pain or discomfort, passing of ascarids by the anus, the mouth or the nose, vomiting, abdominal or epigastric tenderness, fever, constipation, abdominal distention, cough or cold, nausea, headache and diarrhea. Next in order of frequency were convulsions, abnormal pulmonary conditions, anorexia, loss of weight, weakness, malaise, rest-

lessness, abdominal rigidity, palpable abdominal masses, dyspepsia, and dyspnea. There were 18 cases of intestinal obstruction due to Ascariasis reported in this series, 6 of which were fatal. Conditions most frequently confused with Ascariasis were chronic recurrent appendicitis, upper respiratory infection, gastroenteritis, tuberculosis, intestinal obstruction, subacute appendicitis, epilepsy, intussusception and intestinal intoxication. The abdominal pain of *Ascaris* infestation is often recurrent in nature and frequently acute in onset. In many cases it is epigastric or umbilical in location although it may be anywhere. Swartzwelder points out that in over half of his cases the eosinophil count was less than 3 per cent.

This case is reported because of the unusually heavy infestation with *Ascaris lumbricoides* and because of the existing tuberculous infection. It is possible that the former may have rendered the patient less resistant to the invasion of the tubercle bacillus. While heavy infestations are not uncommon in tropical areas, this hospital has no record of similar involvement.

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CLINICOPATHOLOGICAL CONFERENCE

Directed by: E. Clarence Rice, M.D.

Assisted by: Dr. L. Murphy and Dr. F. Leyva

Case Report No. 87

Dr. Francisco Leyva

A ten year old white male was admitted to the Children's Hospital on August 1, 1936 because of back pain of three days duration.

The onset occurred suddenly while he was turning cart-wheels. Examination in the dispensary at that time indicated a probable muscular injury. Hot, moist packs were prescribed but failed to give relief. On the day of admission the pain was severe, and he developed fever and vomiting.

The patient was born at term at home, the birth weight being 11 pounds. He received breast milk, orange juice and cod liver oil in adequate amounts. The developmental history was normal.

Previous diseases included measles, pertussis, chickenpox, frequent colds and an infected laceration of the left hand eight months before the present hospitalization. He had been successfully vaccinated for smallpox and the Schick test was negative at 8 years of age.

One sibling and the parents were living and well. No familial diseases were known.

Physical examination at the time of admission revealed the patient to be a well developed and well nourished white male appearing acutely ill. He lay in bed with a hyperextended spine and flexed lower extremities. The pupils were equal and reacted promptly to light. The ears and nose were normal. The teeth were carious and the tonsils had been enucleated. Expansion of the thorax was normal. Over the right posterior chest the breath sounds were diminished. The apex beat was in the 5th intercostal space and a soft systolic, non-transmitted apical murmur was heard. A slight swelling was noted in the right lumbar area. This region was tender on palpation and dull on percussion. There was obvious pain on flexing the neck and a bilateral positive Kernig sign was elicited. A healing furuncle was present on the left forearm. There was mild cervical, axillary and inguinal lymphadenopathy. The tuberculin test was negative with 0.1 mg. old tuberculin.

The temperature rose to 105° eight hours after admission and ranged from 102° to 105° throughout the illness. The heart rate varied from 110 to 130 per minute and the respirations from 30 to 50 per minute.

During the first 2 days the patient received intravenous fluids, blood transfusions, and sedation. Attempts by x-ray to visualize a localized process in the right lumbar area were unsuccessful. A surgical consultation was requested on the third day because of the persistent tenderness in the right costovertebral angle and over the right rectus muscle anteriorly. Surgical exploration of the perinephritic area by means of an incision in the right lumbar area parallel to the twelfth rib failed to locate any pathological process. A lumbar puncture done at this time obtained 5 cc. of bloody spinal fluid having 2,100 white cells with 96% polymorphonuclear leucocytes and 4% lymphocytes. No organisms were seen on the direct smear. From the culture, gram negative diplococci were reported. Thirty thousand units of meningococcic antitoxin were given intravenously and this was repeated each of the five following days.

The blood count on admission was 21,000 leucocytes with 84% polymorphonuclears of which 2% were band forms. Subsequent leucocyte counts varied between 10,000 and 20,000 with approximately 60% segmented forms and between 17 and 28% band forms. Two out of four specimens of urine contained albumin and acetone but no pus was found. The carbon dioxide combining power varied between 32 and 36 volumes per cent; the non-protein nitrogen ranged between 40 and 45 mg. per cent. One blood culture was reported as showing gram negative cocci. A second bloody spinal fluid grew gram positive cocci. A third cloudy spinal fluid formed a pellicle, had 3,800 leucocytes with 98 per cent polymorphonuclear elements, increased protein and no sugar reduction. A cisternal tap on the eighth day of illness revealed clear fluid, but had 300 leucocytes, increased protein, normal sugar and grew gram positive cocci.

On the sixth day of illness the child was lethargic but responded to questions and took food and fluids by mouth. He complained bitterly of back pain. The abdominal reflexes were absent and no knee or ankle jerks could be obtained. Nuchal rigidity was present and the biceps and triceps reflexes were weak. On the following day the patient began to have attacks of cyanosis requiring oxygen. The pulse became irregular and weak and numerous rales could be heard over the entire lung fields. Twenty thousand additional units of meningococcus antitoxin were given intravenously but the child's course was rapidly downhill and death occurred on the ninth hospital day.

DISCUSSION

Haven W. Mankin: This case appears to be one of meningitis and leaves the type, mode of onset, and explanation of the severe back pain and its role in the disease in question. One must think of a pathological process, rapid in onset, and fulminating in course. The patient apparently was

highly susceptible to infectious processes or low in his resistance to them since he sustained frequent "colds", an infected left hand, and a furuncle on his left forearm within a recent period before hospital admission. The immediate onset may or may not have been caused by the child's doing cart-wheels, but the progressive back pain with other signs and symptoms appearing post-traumatically would lead one to believe that it might be of some importance in this case. There could have been a tuberculous psoas abscess, a subclinical muscular abscess, a transverse process fracture or osteomyelitis of the spine which was aggravated by the gymnastics. A kidney etiology would seem unlikely in view of the back swelling noted, the right rectus muscle tenderness, and the lack of cells in the urine. The surgical intervention should theoretically have revealed the cause of the back pain even if this cause was located in the psoas muscle. The focus, however, may have been so minute as to escape detection while causing severe symptoms. The paucity of pathological findings at operation could be compatible with an osteomyelitis of the spine. This could have been caused by hematogenous spread from the infected left hand or the furuncle on the left forearm. At the time of the physical exertion flexing of the spine may have caused an osteomyelitic process to rupture into the spinal canal and cause a subsequent involvement of the meninges. On the other hand, the complaint in the right posterior lumbar area may have been totally unrelated to the case although this seems improbable.

The meningitis may also have been caused by the rupture of a brain abscess initiated at the time of undue activity. Meningitis is theoretically explainable by direct hematogenous spread from the left forearm furuncle.

In cases of this type the examination of the spinal fluid is mandatory. The findings indicated a purulent meningitis, possibly due to the meningococcus. Evidently this was not the case since 172,000 units of meningococcic antitoxin failed to alleviate the central nervous system symptoms. The course of the disease undoubtedly would have been altered considerably if the chemotherapeutic and antibiotic agents of today were available at that time (1936.)

The bloody taps probably were traumatic although sanguinous spinal fluids are reported with pneumococcus meningitis. The pellicle formation in a single tap is difficult to evaluate. The high cell count with predominant polymorphonuclears, absent sugar and increased protein would indicate bacterial infection.

Tuberculosis must be considered in spite of the negative tuberculin test. In advanced tuberculosis the reaction is occasionally found to be negative. The process in the lumbar region could have been a psoas abscess with involvement of the spine and subsequent tuberculous meningitis.

However, tuberculous meningitis is usually insidious and presents a spinal fluid picture of clear to opalescent fluid, 30 to 1000 lymphocytes, increased protein and decreased sugar. In defense of the cell count it should be mentioned that high cell counts in tuberculous meningitis sometimes reveal a predominance of polymorphonuclear elements. Evidently no x-ray of the chest was taken although there was sufficient clinical evidence to justify this procedure.

I have ruled out meningococcic meningitis on the basis of the poor response to meningococcic antitoxin and the changing culture picture of the spinal fluid although I may be in error to do so. Poliomyelitis and encephalitis are dismissed because of the clinical and spinal fluid findings.

This leaves brain abscess, pneumococcic, staphylococcic or streptococcic meningitis or possibly a mixed infection. Each of these is capable of presenting this picture. Brain abscess on rupture will give the typical findings of a purulent meningitis which is actually the pathogenesis. No cortical symptoms however, are given prominence. I understand that pneumococci upon being cultured, often lose their gram positive characteristics and may be mistaken for gram negative organisms. This possibility might explain the discrepancies found on various cultures.

In view of the difficulty in pinning down this case as to etiology and the mode of onset, it would be desirable to know more about the chest and vertebral column by x-ray. One point against pneumococcic meningitis is the fact that this complication most commonly occurs during an attack of pneumonia or otitis media or shortly thereafter. The streptococcus or staphylococcus would be the likely agents were it not for the finding of gram negative cocci in the spinal fluid and blood stream.

My first diagnosis would be osteomyelitis of the spine with resulting septicemia and meningitis. Ninety per cent of osteomyelitis is caused by the streptococcus and staphylococcus with the latter being the most common cause in older children. Pneumococci are also occasionally the cause. Possibly this is due to a staphylococci although the other two cannot definitely be ruled out. I cannot conclusively dismiss the possibility of brain abscess.

Nicholas Pistolas, M.D.: This seems to be a very interesting and complicating case due to the contradictory remarks concerning the spinal fluid reports, blood culture and failure of surgery to reveal any pathology. If I had examined the child in the out-patient department with the chief complaint of back pain of three days duration following the episode of turning cart-wheels, I too, would have treated the child with rest and hot moist packs to the lumbar region on a basis of a muscular injury. However, since no relief of symptoms was obtained under this regime and the

pain became more severe, associated with complaints of fever and vomiting, I would have admitted the patient for observation.

Two traumatic diagnoses run through my mind immediately: First, fracture subluxation of a lumbar vertebra, and second, ruptured intervertebral disc. The usual case of ruptured intervertebral disc has a much longer history prior to symptomatology and very rarely does swelling and tenderness of a lumbar region manifest itself. Signs of meningeal irritation are never present, as in this case, and we usually find areas of hyperesthesia in the lower extremities. The fulminating and toxic course that this patient followed, along with the spinal fluid findings, certainly makes one dismiss entertaining an intervertebral disc diagnosis. Here again, we can quickly rule out the diagnosis of fracture subluxation of a lumbar vertebra because no complete signs of compression of the cord were present, roentgenograms failed to visualize a lumbar abscess and surely a fracture of a lumbar vertebra in this region would have been noted.

Pain in the right costovertebral angle was his predominant and persistent complaint throughout the entire hospital stay. Surgery was resorted to with the possibility of finding a perinephritic abscess on the right side. Because of the failure to locate any pathological process, I am inclined to make the diagnosis of Pott's disease or tuberculous spondylitis in this particular case, complicated by a tuberculous meningitis, but I do not think that I can do so. It would not be too difficult to visualize a tuberculous osteitis originating in the body of one of the lumbar vertebrae which could destroy the bone and spread to other tissues of articulation, and from this, develop into a psoas abscess. All this could be explained by the physical findings of a hyper-extended spine, flexed lower extremities, tenderness in the right vertebrae angle and over the right rectus muscle anteriorly. But I do not think this is the case since the onset of the disease pursued too rapid a course. The tuberculin test was negative and the x-ray examination of the lumbar area revealed no evidence of any abscess or masses. The obtaining of cloudy spinal fluid, with cell counts of 2,000 and over with a predominance of polys and finding of cocci on culture, help to rule out tuberculous meningitis.

I think we will have to work on the theory that this is a definite purulent meningitis secondary to some focus of infection in the body. Let us not overlook the history of an infected laceration of the left hand 8 months before hospitalization, as well as the finding of a healing furuncle on the left forearm. There is a possibility that a low grade systemic infection was present during the past 8 months which could have flared up with the recent furuncle on the forearm causing a focal suppurative process in either one or both kidneys. Such a process, if walled off in the cortex of the kidney, might not show any urinary changes as was the case here. The

urinary findings could well be explained by dehydration and toxemia. It is not difficult to visualize a purulent meningitis secondary to this suppurative process in the kidney via the hemotogenous route. There are enough physical findings of meningeal and spinal irritation along with cerebro-spinal fluid findings to corroborate this fact. Here we meet with a little controversy concerning the cultures of spinal fluid in which one shows a gram negative diplococci and the other two a gram positive cocci. I do not think that this is a double spinal infection but a single one, and in this case I choose to accept the findings of gram positive cocci instead of gram negative diplococci.

In view of the local signs of infection, central nervous system involvement, low carbon dioxide combining power, findings of gram positive cocci in the spinal fluid and the rapid downhill course of the patient, due to a fulminating blood stream infection, I believe this case to be one of a purulent meningitis (probably staphylococcal in origin) secondary to a focal suppurative process in the kidneys.

NECROPSY FINDINGS

E. Clarence Rice, M.D.: An abscess under the skin of the right chest wall at the level of the third and fourth interspaces was found. The right pleural cavity contained a large amount of clear fluid, a small amount being present in the left. The right lung was adherent posteriorly to the parietal pleura by a fibrino-purulent exudate. The pulmonary tissue was studded with yellow miliary abscesses. The pericardial sac contained a large amount of turbid fluid, the visceral and parietal pericardium being covered with a fibrino-purulent exudate. Several subepicardial abscesses were found. An abscess was found just above the left adrenal. Posterior to the right kidney a considerable amount of greenish yellow pus was noted which extended into the right pelvic region. The last two thoracic and the first lumbar vertebrae were removed and no involvement of the cord found; however, a flow of blood-stained yellow pus appeared from the canal above when the thorax was elevated. The meninges of the brain showed no gross evidence of involvement, although microscopically there was some evidence of meningitis. A staphylococcus was found in smear and culture from the various abscesses.

The anatomical diagnosis was;

1. Abscess of right thoracic wall.
2. Pleural effusion, bilateral.
3. Fibrino-adhesive pleuritis, right.
4. Multiple abscesses of the lung.
5. Acute pericarditis.
6. Subepicardial abscesses.

7. Periadrenal abscess, left.
8. Perinephritic abscess, right.
9. Purulent meningitis.

This case well illustrates the difficulties which may be encountered in staphylococcal infections in children. It is possible that the furuncle noted by the nurse or less likely the lacerated wound eight months previous to hospitalization may have represented the initial infection in this patient.

The bacteriological examination of the blood and spinal fluid gave results which were confusing to the clinicians. Exploratory operation failed to reveal any of the sites of infection which later were found at necropsy.

Such a case is typical of generalized staphylococcal infections in children, the initial lesion usually being an infection in the skin. A number of years ago Conklin(1) reported the deaths of 11 babies who died of *Staphylococcus albus* hemolyticus infection following skin infections acquired in a hospital nursery. Fortunately such infections are less common at the present time due to the availability and use of chemotherapeutic and antibiotic agents. The lesions are usually widely scattered throughout the various organs with a predilection for the lungs. Most perinephritic abscesses are due to the staphylococcus. Of additional interest here was the involvement of the meninges in the thoracic region being evidently embolic in origin, as the brain showed but slight evidence of meningitis, the cisternal fluid having a low cell count compared to the abnormal findings in the spinal fluid indicating more of a spinal than a cerebro-spinal type of meningitis. One would strongly suspect an osteomyelitis involving the vertebrae; however, the necropsy does not describe such a process.

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